Carvalho, Roberta F.; Rosa, Glorimar; Huguenin, Grazielle V. B.; Luiz, Ronir R.; Moreira, Annie S. B.; Oliveira, Glaucia M.M.
The association of selenium status with thyroid hormones and anthropometric values in dyslipidemic patients
Nutrición Hospitalaria, vol. 31, núm. 4, 2015, pp. 1832-1838
Grupo Aula Médica
Madrid, España

Available in: http://www.redalyc.org/articulo.oa?id=309238513050
The association of selenium status with thyroid hormones and anthropometric values in dyslipidemic patients

Roberta F. Carvalho¹, Glorimar Rosa¹,², Grazielle V. B. Huguenin¹, Ronir R. Luiz³, Annie S. B. Moreira¹,⁴ and Glaucia M.M. Oliveira¹

¹Post-graduate Program of Medicine-Cardiology, Federal University of Rio de Janeiro. ¹,²Department of Nutrition and Dietetics, Josué de Castro Nutrition Institute, Federal University of Rio de Janeiro. ¹Institute of Public Health Studies, Federal University of Rio de Janeiro. ¹,⁴Dyslipidemia and Atherosclerosis of Ambulatório, National Institute of Cardiology, Brazil.

Abstract

Background: Selenium (Se) is an essential micronutrient that performs physiological functions in the metabolism of thyroid hormone and may have an association with anthropometric variables relevant to cardiovascular disease. Aim: To study the associations between Se status, thyroid hormones and anthropometric variables in dyslipidemic patients. Methods: Eighty-three patients were assessed in a cross-sectional study. Blood samples were analyzed for Se and thyroid hormones. Anthropometric measurements were taken, and dietary Se intake was investigated.

Results: Mean plasma Se concentrations were low in the patients, at 88.7 ± 16.7 µg/L. Patients with plasma Se ≥ 95 µg/L were found to have a higher body mass index (BMI) (30.74 ± 4.31 vs 27.68 ± 5.63 kg/m², *P* = 0.02) and waist-to-height ratio (0.65 ± 0.05 vs 0.59 ± 0.07, *P* = 0.003) when compared to those with concentrations between 80 and 94 µg/L. Se intake associated positively with T₃L/T₄L ratio (*r* = 0.273; *P* = 0.03), BMI (*r* = 0.257, *P* = 0.04) and WC (*r* = 0.299, *P* = 0.02). Conclusion: The patients with the highest normal plasma Se concentrations were found to have increases in the anthropometric variables we investigated. There is a need for further study in order to elucidate these findings. Furthermore, we found a positive association between Se intake and the most metabolically active form of the thyroid hormones.

(Nutr Hosp. 2015;31:1832-1838)

DOI:10.3305/nh.2015.31.4.8363

Key words: Selenium, Thyroid hormones, Anthropometry, Dyslipidemia.

RELACIÓN ENTRE LOS NIVELES DE SELENIO, LAS HORMONAS TIROIDEAS Y LA ANTROPOMETRÍA EN PACIENTES CON DISLIPIDEMIA

Resumen

Contexto: El selenio (Se) es un micronutriente esencial que realiza las funciones fisiológicas en el metabolismo de la hormona tiroidea y pueden tener una asociación con las variables antropométricas pertinentes a la enfermedad cardiovascular.

Objetivo: Estudiar la asociación entre el estado de Se, hormonas tiroideas y las variables antropométricas en pacientes con dislipidemia.

Métodos: Ochenta y tres pacientes fueron evaluados en un estudio transversal. Se analizaron muestras de sangre para Se y hormonas tiroideas. Las medidas antropométricas fueron tomadas, y la ingesta de la dieta Se fue investigado.

Resultados: La media de las concentraciones de Se en plasma fueron bajas en los pacientes, a 88.7 ± 16.7 mg/L. Se encontró que los pacientes con niveles plasmáticos de Se ≥ 95 mg/L se asociaron con un índice de masa corporal (IMC) (30.74 ± 4.31 vs 27.68 ± 5.63 kg/m², *P* = 0.02) y la relación cintura-estatura (0.65 ± 0.05 vs 0.59 ± 0.07, *P* = 0.003) en comparación con aquellos con concentraciones entre 80 y 94 mg/L. Ingesta de Se asoció positivamente con relación T₃L/T₄L (*r* = 0.273, *P* = 0.03), IMC (*r* = 0.257, *P* = 0.04) y WC (*r* = 0.299, *P* = 0.02). Conclusión: Se encontró que los pacientes con las más altas concentraciones de Se en plasma normal tienen incrementos en las variables antropométricas que investigamos. Hay una necesidad de un mayor estudio para dilucidar estos hallazgos. Además, se encontró una asociación positiva entre el consumo de Se y la forma más metabolícamente activa de las hormonas tiroideas.

(Nutr Hosp. 2015;31:1832-1838)

DOI:10.3305/nh.2015.31.4.8363

Palabras clave: Selenio, Hormonas tiroideas, La antropometría, La dislipidemia.
Introduction

Cardiovascular disease (CVD) is among the main causes of death around the world. The 2010 overall rate of death attributable to CVD in the EUA was 235.5 per 100,000. It is estimated that 23% of the deaths from ischemic heart diseases are related to obesity and overweight2.

Thyroid hormones are related to cardiovascular health3 and, within normal range, have been associated with body weight and waist circumference (WC)4,5. As for the thyroid gland itself, it contains the highest selenium (Se) content of the entire human body6. Se status may have an influence on thyroid hormones7, given its importance in the conversion of the metabolically active form of these hormones and protecting the thyroid gland from the oxidative damage that arises during the synthesis of these hormones8,9.

There is a lack of studies investigating plasma concentrations and intake of Se in association with anthropometric parameters in a dyslipidemic population8,9. Such analysis has clinical relevance due to the importance that changes in body weight have on cardiovascular health2. Our hypothesis is that plasma concentrations, Se intake and thyroid hormones are interrelated, as well as related to anthropometric parameters. The aim of this study, therefore, is to evaluate the association that plasma concentration and intake of Se have with thyroid hormones and anthropometric variables.

Patients and methods

Ethical Concerns

All patients involved in this study were informed of the procedures to which they would be subjected and signed a written consent form. This study was approved by the Clinical Research Ethics Committee of the INC (National Institute of Cardiology) (316/2011).

Patients

Patients were recruited at the National Institute of Cardiology. We studied dyslipidemic patients in the secondary level of health care, all of whom were using lipid-lowering medication.

The entry criteria included euthyroid, dyslipidemic, hypertensive, between 45 and 85 years of age, of both sexes, given overall nutritional orientation by the nutritional outpatient unit, and did not alter the dosage of lipid-lowering medication during the three months prior to joining the study. Subjects were excluded if they had past history of disease or use of thyroid medication; use of medication for treating cardiovascular diseases that affect thyroid function, such as amiodarone and propranolol; having suffered an acute cardiovascular event within the last six months, chronic kidney disease with a glomerular filtration rate < 60 mL/minute/1.73m², or malignancy; use of oral contraceptives or hormone replacement therapy; and participation in a rigorous physical activity/weight loss program during the three months preceding the study.

Of the 97 participants initially recruited over the phone from the INC Atherosclerosis and Cardiovascular Prevention Outpatient Clinic (Rio de Janeiro, Brazil), 83 dyslipidemic and hypertensive patients (49 males and 34 females) were eligible (Fig. 1). Among those who did not meet the inclusion criteria, three were shown to have hyperthyroidism; three, hypothyroidism; two, chronic kidney disease with a glomerular filtration rate < 60 mL/minute/1.73m²; and one was found to have malignancy.

Approach

This was a cross-sectional study between July 2011 and June 2012.

A questionnaire was used to gather information and specifics regarding any medication, practice of physical activities, and dietary habits. Blood samples were taken to determine levels of plasma Se and thyroid hormones, as well as lipid profile. Furthermore, we carried out an anthropometric assessment to determine weight, BMI, waist circumference (WC) and waist-to-height ratio (WHtR).

Analysis of the association, plasma Se and thyroid hormone levels, with anthropometric variables was based on tertiles of study-participant plasma Se concentrations. We also analyzed the associations between Se intake, thyroid hormones and anthropometric variables.

Definitions

Patients were considered dyslipidemic if they were using a lipid-lowering medication or were found to have serum LDL ≥ 160 mg/dL or triglycerides ≥ 150mg/dL or if high-density lipoprotein (HDL) levels were < 40 mg/dL in men and < 50mg/dL in women. These alterations could occur on their own or in association with one another1. Patients were considered to be hypertensive if they were taking antihypertensive drugs or were found to have an average blood pressure ≥ 140/90 mmHg12.

The cutoff points for being classified as having euthyroidism were as follows: TSH of 0.45-4.50 µU/mL; T3L of 0.7-1.48 ng/dL; T3L of 0.58-1.59 ng/mL; T3L of 1.71-3.71 pg/mL13.

Normal plasma Se concentrations were estimated according to levels of the mineral required for attaining maximum glutathione peroxidase activity—a normal range, between 95 and 150 µg/L14. The re-
commended Se intake is 55 µg/day for both sexes, according to Dietary Reference Intake (DRI).\textsuperscript{15}

We define as eutrophic a BMI between 18.5 and 24.9 kg/m\textsuperscript{2}, overweight as a BMI between 25 and 29.9 kg/m\textsuperscript{2}, and obese as a BMI ≥ 30 kg/m\textsuperscript{2}.\textsuperscript{16}

We defining increased WC as being ≥ 88 cm in females and ≥ 102 cm in males\textsuperscript{17}WHtR was considered a determinant of increased coronary risk when ≥ 0.52 in men and ≥ 0.53 in women\textsuperscript{18}.

Questionnaires were employed to assess physical activity\textsuperscript{19}. Individuals were classified as either sedentary, if they practiced no physical activity, or moderately inactive, since none of them was found to expend more than 100 kcal of energy through physical activity per day.

Variables investigated

Body weight was taken using an electronic anthropometric scale (Filizola\textsuperscript{6}, São Paulo, Brazil) with a 180 kg maximum capacity and accurate to 100g. Height measurements were taken using a stadiometer accurate to the 1mm (Standard Sanny\textsuperscript{6}, São Paulo, Brazil). Using the weight and height measurements to calculate it, BMI was defined as weight (kg)/height (m)\textsuperscript{2} (16).

WC was ascertained using measuring tape accurate to the 0.1 cm (Standard Sanny\textsuperscript{6}, São Paulo, Brazil)\textsuperscript{17}, and WHtR was determined by dividing WC (cm) by height (cm)\textsuperscript{18}.

We used WHtR due to its importance as an anthropometric indicator of obesity and predictor of increased coronary risk\textsuperscript{18}.

Fasting blood for biochemical profile was draw after 12-hour fast and was analyzed INC Laboratory for Clinical Analysis (Rio de Janeiro, Brasil) using equipment (ARCHITECT ci8200, Abbott ARCHITECT\textsuperscript{8}, Abbott Park, IL, USA) and commercial kits (Abbott ARCHITECT ci8000\textsuperscript{6}, Abbott Park, IL, USA).

Serum concentrations of TSH and the thyroid hormones total triiodothyronine (T3), free triiodothyronine (T3L) and free thyroxine (T4L) were analyzed using chemiluminescence microparticle immunoassay (CMIA). The free triiodothyronine/free thyroxine ratio (T3L/T4L ratio) was obtained using the conventional units of measure.

Serum concentrations of triglycerides, total cholesterol and HDL-c were determined using the enzymatic colorimetric method: glycerol phosphate oxidase/peroxidase, oxidase/peroxidase cholesterol and direct detergent, respectively. The LDL-c values were obtained using the formula of Friedewald et al. (1972)\textsuperscript{20}.

The plasma Se concentrations were analyzed in samples collected in VACUETTE\textsuperscript{8} Trace Elements NH Sodium Heperin tubes and kept at -70°C until the moment analysis was performed. These concentrations were determined by atomic absorption spectrometry using a mass spectrometer with an inductively coupled plasma source (NexION\textsuperscript{300 ICP-MS, PerkinElmer, Massachusetts, USA). This analysis was carried out at LABSPECTRO, at the Pontific Catholic University of Rio de Janeiro, Brazil.

Habitual dietary Se intake was assessed using a food frequency questionnaire (FFQ) validated\textsuperscript{21} using the Food Processor software version 12 (EshaResearch, 1984, Salem, MA, USA).

Statistical analysis

All results were expressed as mean ± standard deviation (SD) for quantitative variables and as percentages for qualitative variables. We checked for the normality of the variables by using the Kolmogorov-Smirnov statistical test.

We used the Spearman test to analyze the association between Se intake and the variables under study.

When investigating the associations between the plasma Se concentrations in tertiles of the sample population and thyroid hormones and anthropometric variables, we used the Kruskal-Wallis test with a post-hoc Mann-Whitney U test to compare between the two groups. We employed the chi-squared test to assess the difference in prevalence of increased waist circumfe-
The association of selenium status with thyroid hormones and anthropometric values in dyslipidemic patients

A P value < 0.05 was considered statistically significant. Statistical analysis was carried out using SPSS software (version 12, SPSS Inc., Chicago, IL, USA).

Results

Table I shows detailed information on clinical and laboratory variables of the study population. The mean age in the total group was 60.7 ±10.2 years of age. Men and woman were distribute equally (83 patients, 49 of them men). Of them, 33.7% were moderately inactive, while 66.3% were sedentary.

Elevated prevalence of overweight/obese (73.5%), with abdominal obesity with increased WHtRs (n=73, 89%) and increased WC (n=50, 61%). The percentage for adequate BMI was 26.5%, WC was 39%, and WHtR was 11%.

We found that 65.1% of the patients had plasma Se at levels below the baseline values, that is, low concentrations of plasma Se (88.7 ± 16.7 µg/L, minimum: 50 mcg/L and maximum: 122 mcg/L). Additionally, 55% of the patients were found to have Se intake below DRI recommendations.

## Table I

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
<th>Median</th>
<th>Range p25 – p75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Se – µg/L</td>
<td>88.66 ± 16.73</td>
<td>88</td>
<td>78.00 – 101.00</td>
</tr>
<tr>
<td>TSH – µUI/mL</td>
<td>2.55 ± 1.64</td>
<td>2.1</td>
<td>1.52 – 3.21</td>
</tr>
<tr>
<td>T4L – ng/dL</td>
<td>1.19 ± 0.15</td>
<td>1.2</td>
<td>1.11 – 1.29</td>
</tr>
<tr>
<td>T3– ng/mL</td>
<td>1.04 ± 0.21</td>
<td>1</td>
<td>0.92 – 1.19</td>
</tr>
<tr>
<td>T3L – pg/mL</td>
<td>2.94 ± 0.44</td>
<td>2.93</td>
<td>2.68 – 3.19</td>
</tr>
<tr>
<td>T3L/T4L Ratio</td>
<td>2.51 ± 0.49</td>
<td>2.5</td>
<td>2.19 – 2.82</td>
</tr>
<tr>
<td>Total cholesterol – mg/dL</td>
<td>216.87 ± 87.79</td>
<td>205</td>
<td>157.00 – 260.00</td>
</tr>
<tr>
<td>LDL-c – mg/dL</td>
<td>130.95 ± 58.07</td>
<td>118</td>
<td>89.00 – 154.00</td>
</tr>
<tr>
<td>HDL-c – mg/dL</td>
<td>38.65 ± 12.79</td>
<td>35</td>
<td>30.00 – 47.00</td>
</tr>
<tr>
<td>Triglycerides – mg/dL</td>
<td>194.02 ± 131.19</td>
<td>168</td>
<td>120.00 – 235.00</td>
</tr>
<tr>
<td>BMI – kg/m2</td>
<td>29.13 ± 5.02</td>
<td>28.58</td>
<td>25.55 – 32.18</td>
</tr>
<tr>
<td>WC – cm</td>
<td>100.66 ±12.19</td>
<td>99.5</td>
<td>93.50 – 108.00</td>
</tr>
<tr>
<td>WHtR</td>
<td>0.62 ± 0.07</td>
<td>0.62</td>
<td>0.57 – 0.66</td>
</tr>
</tbody>
</table>

Se, selenium; TSH, thyroid stimulating hormone; T4L, free thyroxin; T3, total triiodothyronine; T3L, free triiodothyronine; LDL-c, low density lipoprotein cholesterol; HDL-c, high density lipoprotein cholesterol; BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio.

## Table II

<table>
<thead>
<tr>
<th>Variables</th>
<th>Plasma Se Tertiles</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st tertile (n = 26)</td>
</tr>
<tr>
<td></td>
<td>50 – 79 µg/L</td>
</tr>
<tr>
<td>TSH – µUI/mL</td>
<td>2.50 ± 1.80</td>
</tr>
<tr>
<td>T4L – ng/dL</td>
<td>1.21 ± 0.14</td>
</tr>
<tr>
<td>T3L – pg/mL</td>
<td>2.90 ± 0.52</td>
</tr>
<tr>
<td>T3L/T4L Ratio</td>
<td>2.43 ± 0.57</td>
</tr>
<tr>
<td>BMI – kg/m2</td>
<td>29.03 ± 4.66</td>
</tr>
<tr>
<td>WC – cm*†‡</td>
<td>100.84 ± 10.61</td>
</tr>
<tr>
<td>WHtR*</td>
<td>0.62 ± 0.07</td>
</tr>
</tbody>
</table>

Se, selenium; TSH, thyroid stimulating hormone; T4L, free thyroxin; T3, total triiodothyronine; T3L, free triiodothyronine; BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio.

The variables were presented as mean ± SD. The groups were divided into tertiles according to plasma Se concentrations. To compare the groups, we used the Kruskal-Wallis test due to the abnormal distribution of variables. We used the Mann-Whitney test for analysis between two groups in a post-hoc comparison.

*P < 0.05: 2nd tertile versus 3rd tertile. † P < 0.05: 1st tertile versus 3rd tertile. ‡ P < 0.05: 1st tertile versus 2nd tertile.

The association of selenium status with thyroid hormones and anthropometric values in dyslipidemic patients
The medications used for treating dyslipidemia are presented in Table II. It is noteworthy that most of the patients were taking statins.

Se intake associated positively with T3L/T4L ratio ($r = 0.273$, $P = 0.03$), BMI ($r = 0.257$, $P = 0.04$) and WC ($r = 0.299$, $P = 0.02$).

The differences between the tertiles of plasma Se concentrations and the serum thyroid hormone levels and anthropometric variables are presented in Table III.

No differences in TSH concentrations, thyroid hormones or T3L/T4L ratio were found between the groups according to plasma Se concentrations (Table III).

Patients belonging to the group with the highest plasma Se concentrations were found to have the highest BMI ($P = 0.02$), WC ($P < 0.001$) and WHtR ($P = 0.003$) when compared to those with intermediate concentrations. Moreover, the patients in the 1st plasma Se tertile too had a higher WC compared to the group with the intermediate concentrations ($P = 0.03$), despite the patients belonging to the 1st tertile showing a lower WC when compared to those of the 3rd tertile ($P = 0.04$) (Table III).

Figure 2 features the prevalence of increased WC by plasma Se-concentration tertiles.

![Figure 2](image)

**Figure 2.** Prevalences of increases (%) in Waist Circumference (WC) according to tertiles of plasma Se concentrations. The prevalence of increased WC was least in the group with intermediate Se concentrations ($P = 0.001$).

**Table III**

<table>
<thead>
<tr>
<th>Lipid-lowering drugs</th>
<th>Drug therapy – no</th>
<th>Combination of medications – no*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statins</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Fibrates</td>
<td>29</td>
<td></td>
</tr>
</tbody>
</table>

* Number of patients using a combination of two or more oral medications.

Discussion

In this cross-sectional study, we found plasma Se concentrations were low, given how 95 to 150 µg/L was considered to be the optimal range for plasma Se concentrations in the dyslipidemic and hypertensive patients. This can be explained by the low dietary intake of Se. Furthermore, the increase in oxidative stress inherent in dyslipidemia, which causes a rise in demand for glutathione peroxidase and other antioxidant selenoproteins, may possibly have a role in this finding. There are some studies in dyslipidemic patients that show low plasma Se concentrations, between 55 and 88 µg/L. Another significant aspect comes from a cross-sectional study by Arnaud et al. (2008), they found the use of statin treatment in dyslipidemic patients takes to a lower plasma Se concentrations than those taking fibrates, the average plasma Se concentrations being 75.8 and 87.7 µg/L, respectively. However, no difference in plasma Se values was found between the groups that were given statins, fibrates or who didn’t take oral lipid-lowering medication after nine years of accompaniment.

Dietary Se intake undergoes great variability worldwide because of its content in the soil and the diversity of eating habits. Maihara et al. (2004) demonstrated that in Brazil dietary Se intake varies from 19 to 94.5 µg per day, depending on the region.

The positive associations between Se intake, BMI, WC and higher BMI, WC and WHtR values in the group of patients with higher plasma Se concentrations can be attributed to the alterations induced in energy metabolism, as demonstrated by Pinto et al. (2012) in their study on animals. In this study, a rise in plasma Se resulted in an increase in GP (x) activity and a decrease in the genetic expression of enzymes involved in energy metabolism, such as AMP-activated kinase and the glycolytic enzyme pyruvate kinase. Thus, Se supplementation would tend to block the oxidation of glucose while increasing the oxidation of fatty acids, altering the source of energy and the physiological metabolism of the individual, which could lead to an increase in body weight. A study on
The association of selenium status with thyroid hormones and anthropometric values in dyslipidemic patients

Nutr Hosp. 2015;31(4):1832-1838

Acknowledgments

This study was funded in part by the FAPERJ (Foundation for Research Support of the State of Rio de Janeiro) - number E-26/112.182/2012. CAPES (Government agency linked to the Brazilian Ministry of Education in charge of promoting high standards for post-graduate courses in Brazil) We thank Rachel Ann Hauser-Davis, Rafael Christian Chávez Rocha and Alvaro Jorge Pereira for their assistance with the Se analysis, and Nena Coelho, Francis Ribeiro and Mário Gonzalez for the facilities they made available at the INC.

References